

Ex. 3

CD4

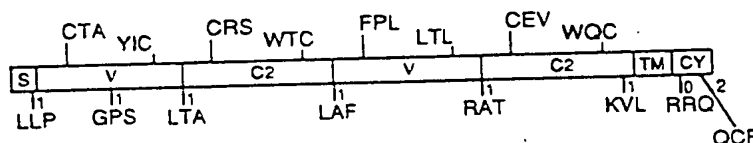
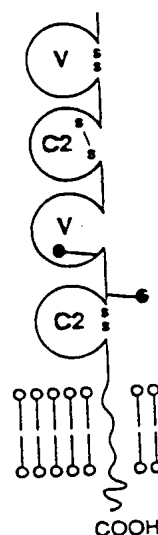
T4, L3T4 (mouse), W3/25 (rat)

Molecular weights
Polypeptide 48400

SDS PAGE
reduced 55 kD
unreduced 55 kD

Carbohydrate
N-linked sites 2
O-linked nil

Human gene location and size
12pter-p12; 33 kb¹



Tissue distribution

CD4 is expressed on most thymocytes and approximately two thirds of peripheral blood T cells, which constitute the CD8 negative cells². In human and rat but not in mouse, CD4 is expressed on monocytes and macrophages².

Structure

The extracellular domain is made up of four IgSF domains. The structures of the amino terminal two domains have been determined by X-ray crystallography, confirming that they are Ig-like^{3,4}. Domain 2 is characterized by an unusual disulphide within one beta sheet and domain 3 lacks a disulphide in the position conserved in most IgSF domains. Cat CD4 shows some unusual features with 17 residues inserted between domains 1 and 2⁵. There is an additional Cys in domain 1 and the Cys in the unusual β strand C position in domain 2 is replaced with a Trp and there is an extra Cys in the β strand F⁵. The position of the NH₂-terminus has been established for the rat homologue⁶.

Function

CD4 is an accessory molecule in the recognition of foreign antigens in association with MHC Class II antigens by T cells². MAbs against CD4

inhibit T cell functions *in vivo* and *in vitro* ². The cytoplasmic domain of CD4 is phosphorylated at Ser residues 408, 415, 431 (see below) when T cells are activated by antigen or phorbol esters ⁷. The cytoplasmic domain interacts with a lymphocyte-specific tyrosine kinase called p56^{lck} through a motif shown below ⁸. CD4 is a receptor for HIV-1 (AIDS virus) and the binding of the viral gp120 protein is to a region of the amino terminal domain ^{3,4}.

Comments

CD4 shows particularly close similarities in overall structure to the LAG-3 protein (see page 342).

Motifs involved in CD4 function

p56^{lck} recognition site (underlined) and Ser residues phosphorylated (in bold)
RRQAERMSQI KRLLSEKKTC QCPHRFOKTC SPI (433)

Database accession numbers

	PIR	SWISSPROT	EMBL/GENBANK	REFERENCE
Human	AO2109	P01730	M12807	2
Rat	A27449	P05540	M15768	6
Mouse	A02110	P06332	M13816	2

Amino acid sequence of human CD4

MNRGVPFRHL	LLVLQLALLP	AATQG	-1
KKVVLGKKGD	TVELTCTASQ	KKSIOFHWKN	50
LNDRADSRRS	LWDQGNFPLI	IKNLKIEDSD	100
TANS DTHLLO	GSLTLTLLES	PPGSSPSVQC	150
LQDSGTWTCT	VLONOKKVEF	KIDIVVLAFO	200
AFTVEKLTGS	GELWQOAERA	SSSKSWITFD	250
KKLPLHLTLP	QALPOYAGSG	NLTALAEAKT	300
LTCEVWGPTS	PKMLLSLKLE	NKEAKVSKRE	350
GOVLLESNIK	VLPTWSTPVQ	PMALIVLGGV	400
RRQAERMSQI	KRLLSEKKTC	QCPHRFOKTC SPI	433

References

- Maddon, P.J. et al. (1987) Proc. Nat Acad. Sci. USA 84, 9155-9159.
- Parnes, J.R. (1989) Adv. Immunol. 44, 265-311.
- Wang, J. et al. (1990) Nature 348, 411-418.
- Ryu, S-E. et al. (1990) Nature 348, 419-426.
- Norimine, J. et al. (1992) Immunology 75, 74-79.
- Clark, S.J. et al. (1987) Proc. Natl Acad. Sci. USA 84, 1649-1653.
- Shin, J. et al. (1990) EMBO J. 9, 425-434.
- Turner, J.M. et al. (1990) Cell 60, 755-757.